SEQUENCE LISTING

<110> KYOWA HAKKO KOGYO CO., LTD

<120> AGENT FOR TREATING ARTHRITIS

<130> 1442

<150> JP2001-400677
<151> 2001-12-28

<160> 51

<170> PatentIn version 3.1

<210> 1
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<212> DNA

<213> Mus musculus

<220>
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<222> (1)..(420)
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<220>
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<220>
<221> sig_peptide
<222> (1)..(57)

<400> 1

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atg gaa tgg atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt       48
Met Glu Trp Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly
  1               5                  10                  15

gtc tac tcc cag gtt cag ctg cag cag tct gga gct gag gtg gcg agg       96
Val Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg
             20                  25                  30

ccc ggg gct tca gtg aaa ctg tcc tgc aag gct tct ggc tac acc ttc      144
Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe
         35                  40                  45

act gac tac tat cta aac tgg gtg aag cag agg tct gga cag ggc ctt      192
Thr Asp Tyr Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu
     50                  55                  60

gag tgg att gga gag att gat cct gga agt gat agt ata tat tat aat      240
Glu Trp Ile Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn
 65                  70                  75                  80
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gaa aac ttg gag ggc agg gcc aca ctg act gca gac aaa tcc tcc agc      288
Glu Asn Leu Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser
                85                  90                  95

aca gcc tac atg cag ctc aac agc ctg aca tct gag gac tct gca gtc      336
Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
            100                 105                 110

tat ttc tgt gca aga tat ggg tat tct aga tac gac gta agg ttt gtc      384
Tyr Phe Cys Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val
        115                 120                 125

tac tgg ggc caa ggg act ctg gtc act gtc tct aca                      420
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Thr
    130                 135                 140
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<210> 2
<211> 140
<212> PRT
<213> Mus musculus

<220>
<221> SIGNAL
<222> (1)..(19)

<400> 2

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Met Glu Trp Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly
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Val Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg
             20                  25                  30

Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe
         35                  40                  45

Thr Asp Tyr Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu
     50                  55                  60

Glu Trp Ile Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn
 65                  70                  75                  80

Glu Asn Leu Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser
                85                  90                  95

Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
            100                 105                 110

Tyr Phe Cys Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val
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```
        115                 120                 125

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Thr
    130                 135                 140


<210>  3
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<213>  Mus musculus

<220>
<221>  source
<222>  (1)..(393)
<223>  /organism="Mus musculus"

<220>
<221>  CDS
<222>  (1)..(393)

<220>
<221>  sig_peptide
<222>  (1)..(57)

<400>  3
atg aag ttg cct gtt agg ctg ttg gtg ctg atg ttc tgg att cct gct       48
Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala
  1               5                  10                  15

tcc agg agt gat gtt ttg atg acc caa act cca ctc tcc ctg cct gtc       96
Ser Arg Ser Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val
             20                  25                  30

agt ctt gga gat caa gcc tcc atc tct tgc aga tct agt cag agt ctt      144
Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
         35                  40                  45

gta cat agt aat gga aga acc tat tta gaa tgg tac ctg cag aaa cct      192
Val His Ser Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro
     50                  55                  60

ggc cag tca cca aag gtc ctg atc tac aaa gtt tcc aac cga att tct      240
Gly Gln Ser Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser
 65                  70                  75                  80

ggg gtc cca gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca      288
Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
                 85                  90                  95

ctc aaa atc agc aga gtg gag gct gag gat ctg gga gtt tat ttc tgc      336
Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
            100                 105                 110

ttt cag ggt tca cat gtt ccg tac acg ttc gga ggg ggg acc aag ctg      384
Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
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        115                 120                 125

gaa ata aaa                                                         393
Glu Ile Lys
    130


<210>  4
<211>  131
<212>  PRT
<213>  Mus musculus

<220>
<221>  SIGNAL
<222>  (1)..(19)

<400>  4
Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala
  1               5                  10                  15

Ser Arg Ser Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val
             20                  25                  30

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
         35                  40                  45

Val His Ser Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro
     50                  55                  60

Gly Gln Ser Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser
 65                  70                  75                  80

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
                 85                  90                  95

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
            100                 105                 110

Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
        115                 120                 125

Glu Ile Lys
    130


<210>  5
<211>  121
<212>  PRT
<213>  Mus musculus

<400>  5
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala
  1               5                  10                  15


Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
             20                  25                  30
```

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Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
         35                  40                  45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
     50                  55                  60

Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65                  70                  75                  80

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                 85                  90                  95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Thr
        115                 120
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<210> 6
<211> 112
<212> PRT
<213> Mus musculus

<400> 6

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Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
  1               5                  10                  15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
             20                  25                  30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
         35                  40                  45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
     50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe Gln Gly
                 85                  90                  95

Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
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100 105 110

<210> 7
<211> 5
<212> PRT
<213> Mus musculus

<400> 7
Asp Tyr Tyr Leu Asn
1 5

<210> 8
<211> 17
<212> PRT
<213> Mus musculus

<400> 8
Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu Glu
1 5 10 15

Gly

<210> 9
<211> 12
<212> PRT
<213> Mus musculus

<400> 9
Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr
1 5 10

<210> 10
<211> 16
<212> PRT
<213> Mus musculus

<400> 10
Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Arg Thr Tyr Leu Glu
1 5 10 15

<210> 11
<211> 7
<212> PRT
<213> Mus musculus

<400> 11
Lys Val Ser Asn Arg Ile Ser
1 5

<210> 12

<211> 9
<212> PRT
<213> Mus musculus

<400> 12
Phe Gln Gly Ser His Val Pro Tyr Thr
1 5

<210> 13
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VH

<400> 13
ctgaattcgc ggccgctagt cc 22

<210> 14
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VH

<400> 14
atgggccctt ggtggaggct gtagagacag tgaccagag 39

<210> 15
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VL

<400> 15
ctgaattcgc ggccgctgct gt 22

<210> 16
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for amplification of KM1334 VL

<400> 16
atcgtacgtt ttatttccag cttggtcc 28

<210> 17
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> human FGF-8 peptide (amino acis residues 23-46) added an cystein residue at its C-terminus

<400> 17
Gln Val Thr Val Gln Ser Ser Pro Asn Phe Thr Gln His Val Arg Glu
1 5 10 15

Gln Ser Leu Val Thr Asp Gln Leu Cys
20 25

<210> 18
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> HV.0, a designed amino acid sequence of VH of an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 18
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 19
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.0, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 19
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 20
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> HV.6, a designed amino acid sequence of VH of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 20
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Leu Asn Trp Val Arg Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 21
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.6, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 21
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

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Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105                 110


<210>  22
<211>  504
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  a DNA encoding HV.0

<220>
<221>  CDS
<222>  (47)..(466)

<220>
<221>  sig_peptide
<222>  (47)..(103)

<400>  22
caggaaacag ctatgacgaa ttcgcggccg cacactgact ctaacc atg gaa tgg        55
                                                 Met Glu Trp

atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt gtc tac tcc      103
Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly Val Tyr Ser
    -15                 -10                 -5                  -1

cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag ccc ggg gcc      151
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
  1               5                  10                  15

tca gtg aag gtc tcc tgc aag gct tct gga tac acc ttc act gac tac      199
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30

tat cta aac tgg gtg cgg cag gcc ccc gga caa ggg ctt gag tgg atg      247
Tyr Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

gga gag atc gat cct gga agt gat agt ata tat tat aat gaa aac ttg   295
Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
    50                  55                  60

gag ggc aga gtc acg att acc gcg gac aca tcc acg agc aca gcc tac   343
Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat tac tgt   391
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

gcg aga tat ggg tat tct aga tac gac gta agg ttt gtc tac tgg ggc   439
Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
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100 105 110

cag gga acc ctg gtc acc gtc tcc tca gcctccacca agggcccact 486
Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

agtcgtgact gggaaaac 504

<210> 23
<211> 141
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 23
caggaaacag ctatgacgaa ttcgcggccg cacactgact ctaaccatgg aatggatctg 60

gatctttctc ttcttcctct caggaactac aggtgtctac tcccaggtgc agctggtgca 120

gtctggggct gaggtgaaga a 141

<210> 24
<211> 141
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 24
aggatcgatc tctcccatcc actcaagccc ttgtccgggg gcctgccgca cccagtttag 60

atagtagtca gtgaaggtgt atccagaagc cttgcaggag accttcactg aggccccggg 120

cttcttcacc tcagccccag a 141

<210> 25
<211> 141
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 25
ggatgggaga gatcgatcct ggaagtgata gtatatatta taatgaaaac ttggagggca 60

gagtcacgat taccgcggac acatccacga gcacagccta catggagctg agcagcctga 120

gatctgagga cacggccgtg t 141

<210> 26
<211> 141
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 26
gttttcccag tcacgactag tgggcccttg gtggaggctg aggagacggt gaccagggtt 60

ccctggcccc agtagacaaa ccttacgtcg tatctagaat acccatatct cgcacagtaa 120

tacacggccg tgtcctcaga t 141

<210> 27
<211> 504
<212> DNA
<213> Artificial Sequence

<220>
<223> a DNA encoding HV.6

<220>
<221> CDS
<222> (47)..(466)

<220>
<221> sig_peptide
<222> (47)..(103)

<400> 27
caggaaacag ctatgacgaa ttcgcggccg cacactgact ctaacc atg gaa tgg 55
Met Glu Trp

atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt gtc tac tcc 103
Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly Val Tyr Ser
-15 -10 -5 -1

cag gtg cag ctg gtg cag tct ggg gct gag gtg gcg agg ccc ggg gcc 151
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala
1 5 10 15

tca gtg aag gtc tcc tgc aag gct tct gga tac acc ttc act gac tac 199
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

tat cta aac tgg gtg cgg cag agg tct gga caa ggg ctt gag tgg att 247
Tyr Leu Asn Trp Val Arg Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile
35 40 45

gga gag atc gat cct gga agt gat agt ata tat tat aat gaa aac ttg 295
Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

```
gag ggc aga gtc acg att acc gcg gac aca tcc acg agc aca gcc tac      343
Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65                  70                  75                  80

atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat ttc tgt      391
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys
                 85                  90                  95

gcg aga tat ggg tat tct aga tac gac gta agg ttt gtc tac tgg ggc      439
Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
            100                 105                 110

cag gga acc ctg gtc acc gtc tcc tca  gcctccacca agggcccact          486
Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120

agtcgtgact gggaaaac                                                 504


<210>  28
<211>  141
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  a synthetic DNA for construction of a DNA encoding HV.6

<400>  28
caggaaacag ctatgacgaa ttcgcggccg cacactgact ctaaccatgg aatggatctg     60

gatctttctc ttcttcctct caggaactac aggtgtctac tcccaggtgc agctggtgca    120

gtctggggct gaggtggcga g                                             141


<210>  29
<211>  141
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  a synthetic DNA for construction of a DNA encoding HV.6

<400>  29

aggatcgatc tctccaatcc actcaagccc ttgtccagac ctctgccgca cccagtttag     60

atagtagtca gtgaaggtgt atccagaagc cttgcaggag accttcactg aggccccggg    120

cctcgccacc tcagccccag a                                             141


<210>  30
<211>  141
<212>  DNA
<213>  Artificial Sequence
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<220>
<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 30
ggattggaga gatcgatcct ggaagtgata gtatatatta taatgaaaac ttggagggca 60

gagtcacgat taccgcggac acatccacga gcacagccta catggagctg agcagcctga 120

gatctgagga cacggccgtg t 141

<210> 31
<211> 141
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 31
gttttcccag tcacgactag tgggcccttg gtggaggctg aggagacggt gaccagggtt 60

ccctggcccc agtagacaaa ccttacgtcg tatctagaat acccatatct cgcacagaaa 120

tacacggccg tgtcctcaga t 141

<210> 32
<211> 459
<212> DNA
<213> Artificial Sequence

<220>
<223> a DNA encoding LV.0

<220>
<221> CDS
<222> (40)..(432)

<220>
<221> sig_peptide
<222> (40)..(96)

<400> 32

caggaaacag ctatgacgaa ttcaggttgc ctcctcaaa atg aag ttg cct gtt 54
Met Lys Leu Pro Val
-15

agg ctg ttg gtg ctg atg ttc tgg att cct gct tcc agg agt gat atc 102
Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala Ser Arg Ser Asp Ile
-10 -5 -1 1

gtg atg act cag tct cca ctc tcc ctg ccc gtc acc cct gga gag ccg 150
Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
5 10 15

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gcc tcc atc tcc tgc aga tct agt cag agt ctt gta cat agt aat gga      198
Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly
     20                  25                  30

aga acc tat tta gaa tgg tac ctg cag aag cca ggc cag tct cca cag      246
Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
 35                  40                  45                  50

ctc ctg atc tat aaa gtt tcc aac cga att tct ggg gtc cca gac agg      294
Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro Asp Arg
                 55                  60                  65

ttc agt ggc agt gga tcc ggg aca gat ttc aca ctg aaa atc agc agg      342
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
             70                  75                  80

gtg gag gct gag gac gtc ggg gtt tat tac tgc ttt cag ggt tca cat      390
Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly Ser His
         85                  90                  95

gtt ccg tac acg ttc ggc caa ggg acc aag gtg gaa atc aaa              432
Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    100                 105                 110

cgtacgacta gtcgtgactg ggaaaac                                       459
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<210> 33
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 33
caggaaacag ctatgacgaa ttcaggttgc ctcctcaaaa tgaagttgcc tgttaggctg 60

ttggtgctga tgttctggat tcctgcttcc aggagtgata tcgtgatgac tcagtctcca 120

ctctccctgc 130

<210> 34
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 34
agactggcct ggcttctgca ggtaccattc taaataggtt cttccattac tatgtacaag 60

actctgacta gatctgcagg agatggaggc cggctctcca ggggtgacgg gcagggagag 120

tggagactga 130

<210> 35
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 35
tgcagaagcc aggccagtct ccacagctcc tgatctataa agtttccaac cgaatttctg 60

gggtcccaga caggttcagt ggcagtggat ccgggacaga tttcacactg aaaatcagca 120

gggtggaggc 130

<210> 36
<211> 129
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 36
gttttcccag tcacgactag tcgtacgttt gatttccacc ttggtccctt ggccgaacgt 60

gtacggaaca tgtgaaccct gaaagcagta ataaaccccg acgtcctcag cctccaccct 120

gctgatttt 129

<210> 37
<211> 459
<212> DNA
<213> Artificial Sequence

<220>
<223> a DNA encoding LV.6

<220>
<221> CDS
<222> (40)..(432)

<220>
<221> sig_peptide
<222> (40)..(96)

<400> 37
caggaaacag ctatgacgaa ttcaggttgc ctcctcaaa atg aag ttg cct gtt 54
Met Lys Leu Pro Val
-15

agg ctg ttg gtg ctg atg ttc tgg att cct gct tcc agg agt gat gtt 102
Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala Ser Arg Ser Asp Val

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                -10                 -5              -1   1

gtg atg act cag tct cca ctc tcc ctg ccc gtc agt ctt gga gag ccg      150
Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly Glu Pro
          5                  10                  15

gcc tcc atc tcc tgc aga tct agt cag agt ctt gta cat agt aat gga      198
Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly
     20                  25                  30

aga acc tat tta gaa tgg tac ctg cag aag cca ggc cag tct cca aag      246
Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys
 35                  40                  45                  50

gtc ctg atc tat aaa gtt tcc aac cga att tct ggg gtc cca gac agg      294
Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro Asp Arg
                 55                  60                  65

ttc agt ggc agt gga tcc ggg aca gat ttc aca ctg aaa atc agc agg      342
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
             70                  75                  80

gtg gag gct gag gac gtc ggg gtt tat ttc tgc ttt cag ggt tca cat      390
Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly Ser His
         85                  90                  95

gtt ccg tac acg ttc ggc caa ggg acc aag gtg gaa atc aaa               432
Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
    100                 105                 110

cgtacgacta gtcgtgactg ggaaaac                                        459


<210>  38
<211>  130
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  a synthetic DNA for construction of a DNA encoding LV.6


<400>  38
caggaaacag ctatgacgaa ttcaggttgc ctcctcaaaa tgaagttgcc tgttaggctg     60

ttggtgctga tgttctggat tcctgcttcc aggagtgatg ttgtgatgac tcagtctcca    120

ctctccctgc                                                           130


<210>  39
<211>  130
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  a synthetic DNA for construction of a DNA encoding LV.6
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<400> 39
agactggcct ggcttctgca ggtaccattc taaataggtt cttccattac tatgtacaag 60

actctgacta gatctgcagg agatggaggc cggctctcca agactgacgg gcagggagag 120

tggagactga 130

<210> 40
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 40
tgcagaagcc aggccagtct ccaaaggtcc tgatctataa agtttccaac cgaatttctg 60

gggtcccaga caggttcagt ggcagtggat ccgggacaga tttcacactg aaaatcagca 120

gggtggaggc 130

<210> 41
<211> 129
<212> DNA
<213> Artificial Sequence

<220>
<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 41
gttttcccag tcacgactag tcgtacgttt gatttccacc ttggtccctt ggccgaacgt 60

gtacggaaca tgtgaaccct gaaagcagaa ataaaccccg acgtcctcag cctccaccct 120

gctgatttt 129

<210> 42
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.4-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 42
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser

20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 43
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.4-2, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 43
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 44
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.3-1, a designed amino acid sequence of VL of an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 44
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 45
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.3-2, a designed amino acid sequence of VL of an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 45
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser

20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 46
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.2-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 46
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 47
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.2-2, a designed amino acid sequence of VL of an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 47
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 48
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for construction of DNA encoding LV.3-1

<400> 48
atggtacctg cagaagccag gccagtctcc acaggtcct 39

<210> 49

<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer for construction of DNA encoding LV.2-2

<400> 49
atggtacctg cagaagccag gccagtctcc acagctcct 39

<210> 50
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.4-3, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 50
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 51
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> LV.3-3, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 51

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Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
 1               5                  10                  15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
                85                  90                  95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
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